

# Radical Peritoneal Debridement for Established Peritonitis

## The Results of a Prospective Randomized Clinical Trial

HIRAM C. POLK, JR., M.D., DONALD E. FRY, M.D.

A randomized, prospective comparison of radical peritoneal debridement and standard surgical management of peritonitis disclosed no differences in terms of hospital mortality or the frequency of reoperation for abscess. Adjunctive measures such as antibiotic therapy and peritoneal irrigation were identical between the groups. The groups were demographically and clinically similar but had a much lower incidence of intestinal obstruction than in the patients originally reported by Hudspeth.

SECONDARY BACTERIAL PERITONITIS continues as a frequent cause of death and disability in all age groups. The risk of untoward outcome remains a function of basic disease, the organ which has perforated, the duration of illness, and patient resiliency, largely expressed as age and frequency of associated disease. The impact of treatment innovations is difficult to assess objectively. Present therapy embodies adequate parenteral therapy, including systemic antibiotics, initiated as soon as the diagnosis is made<sup>2,3</sup> and early operation with appropriate mechanical management of the alimentary perforation. The roles of peritoneal irrigation and/or continuing lavage<sup>6,7,13-15</sup> with or without specific antimicrobial agents<sup>18</sup> and drainage processes continue to be variable<sup>16</sup> and somewhat controversial.

For all of these reasons, treatment regimens or concepts that appear to favorably influence this prevalent illness are worthy of careful scrutiny. A case in point is the indication by Hudspeth<sup>11</sup> that radical surgical debridement of peritoneal and serosal surfaces, in addition to sound supportive measures and precise mechanical correction of the primary problem, led to uniform recovery in 92 consecutive patients aged three to 69 years. Only 32 of his patients had appendiceal disease and the majority had more serious underlying pathology. This report was greeted with general but unofficial skepticism. His rational was that residual

*From the Department of Surgery and the Price Institute of Surgical Research, University of Louisville School of Medicine and Veterans Administration Medical Center, Louisville, Kentucky*

bacteria-laden fibrinous exudate within the peritoneal cavity serves as a focus of continuing bacterial proliferation and on-going invasive infection. Furthermore, a series of careful experimental studies by Hau and associates<sup>9</sup> provided a reasonable basis by which debridement of fibrinous exudates at some stage in the evaluation of peritonitis could be appreciated as theoretic and practical benefit.<sup>1,9,10,12</sup> Simply stated, Hau and his colleagues suggest that fibrin deposition lowers early mortality in peritonitis by "trapping" bacteria, but that this same protective element of host defenses may become a source for the subsequent development of intraperitoneal abscess. This concept implies that removal of that fibrin "peel" in certain clinical circumstances could be of measurable benefit, as described by Hudspeth.<sup>11</sup> We sought to define the benefits of radical peritoneal debridement in a prospective, randomized study of peritonitis.

### Materials and Methods

During an 18-month period of time, consecutive patients seen at a city-county general hospital and a VA Medical Center with acute bacterial peritonitis were considered candidates for randomization into the study. Sixty adult patients were randomized and at operation, 14 patients were excluded because no peritonitis was encountered or only localized and nondiffuse peritoneal infection was present. All patients entered into the study were randomized, prior to operative intervention, into the radical peritoneal debridement group (RPD) or standard treatment group (STD) based upon the last digit of the hospital number, a number not amenable to manipulation by the treating physician.

The STD patients had a conventional operative

Presented at the Annual Meeting of the American Surgical Association, Atlanta, Georgia, April 23-25, 1980.

Reprint requests: Hiram C. Polk, Jr., M.D., Department of Surgery, University of Louisville School of Medicine, Louisville, Kentucky 40201.

incision based on the suspected diagnosis. For example, patients with suspected perforative appendicitis usually had an oblique right lower quadrant incision. These patients had conventional treatment of repair, resection, and/or exteriorization of the gastrointestinal lesion with conventional suctioning of gross exudate, drainage of purulent collections, and debridement of necrotic tissue. Drains were employed as warranted by the operating surgeon.

The RPD patients all had xiphoid-to-symphysis pubis midline incisions, regardless of the anticipated primary diagnosis. Conventional mechanical treatment objectives were accomplished as in the STD patients. However, RPD patients underwent the meticulous dissection of fibrinous debris and exudate that was adherent to bowel serosa or the parietal peritoneum. This was most conveniently done by gentle, sweeping motions with a coarse-mesh gauze sponge. When the fibrinous exudate was densely adherent or intertwined with the bowel serosa, very careful sharp dissection was employed to avoid subsequent fistulization. No drains were employed in RPD patients.

All patients in both groups were otherwise treated similarly to minimize variables and maximize comparability of the groups. Thorough preoperative history and physical examination allowed assessment of associated disease problems. Antibiotic therapy was initiated preoperatively and all patients received cefamandole nafate 1 g every four hours intravenously and tobramycin 3–4 mg/kg/24 hours intramuscularly. All patients received the drugs preoperatively and for a minimum of five days. The regimen chosen has both

TABLE 1. Demographic Characteristics

Treatment Plans	RPD	STD
Randomized	31	29
Peritonitis not confirmed	9	5
Treated per protocol	22	24
mean age (years)	49	51
sex (male/female)	17/5	17/7
Peritonitis		
localized	7	10
generalized	15	14

theoretic and proven clinical value for peritonitis.<sup>19,20</sup> Drugs could be changed after that point based on culture and sensitivity data. At operation, management of the primary lesion was left to the discretion of the operating surgeon. Aerobic and anaerobic cultures were obtained on opening the peritoneal cavity. Irrigation of the peritoneal cavity was performed in all patients with a minimum of 2,000 ml of warm saline. Additional volume could be employed if the operating surgeon chose to do so. However, no antiseptics nor antibiotics were added to the peritoneal irrigation solutions. Continuous peritoneal irrigation was not employed. Management of the operative wound was left to the surgeon's discretion but delayed primary closure was uniformly chosen.

The major criterion for comparison between the two treatment groups was in-hospital mortality. In addition, reoperation for recurrent intra-abdominal abscess not associated with a technical or judgment error on the part of the operating surgeon was also used in comparing the treatment methods.

### Results

Among the 46 determinant patients, 22 individuals underwent RPD and 24 had standard surgical treatment (STD). The mean age of RPD patients was 49 years and for STD patients 51 years; the age distribution was also similar (Fig. 1). There were 17 men in each group (Table 1). Associated illnesses were common and represent those commonly seen in city-county and Veterans Administration Medical Center hospitals. Alcoholism, atherosclerotic cardiovascular disease and chronic lung disease were most common (Table 2).

The fundamental pathology is tabulated in Table 3. Perforated peptic ulcers and complicated perforative appendicitis accounted for two-thirds of the diagnoses. With a single exception in each therapeutic group, the remaining patients had small or large bowel perforations. The other RPD patient had a ruptured tubo-ovarian abscess and one STD patient had a ruptured pancreatic abscess. The bacteriologic isolates for each treatment group are detailed in Table 4. The aerobic and anaerobic distributions are similar although there are minor variations among the specific organisms.

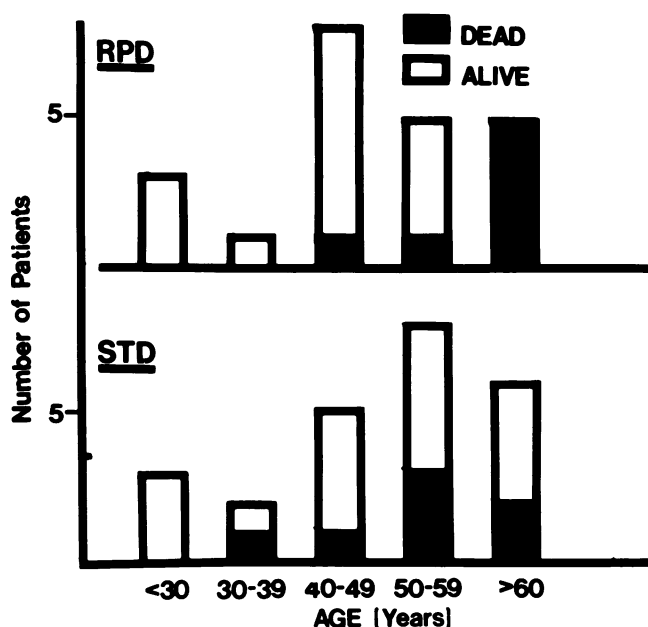


FIG. 1. Distribution of patients according to age and hospital mortality.

TABLE 2. Associated Diseases

Treatment Plan	RPD	STD
Number of patients	22	24
Alcoholism	7	9
Atherosclerotic cardiovascular	6	4
Chronic lung	3	4
Other to include peptic ulcer, diabetes mellitus, chronic renal disease, etc.	8	10
Total associated diseases	24	27

Three patients in the RPD group and five in the STD group had sterile cultures, all of which occurred with perforated duodenal ulcers.

Objective measurements of outcome (Table 5) demonstrate no difference between the treatments as practiced in this population. Of the 24 STD patients, seven died and four required reoperation for intra-abdominal abscess. Of the seven STD deaths, six were due to continuing intraperitoneal infection and one to pneumonia. Seven of the 22 RPD patients died and five required reoperation for intra-abdominal abscess. Of the seven deaths, five were due to peritonitis, one pneumonia, and one from the systemic manifestations of metastatic cancer.

Figure 1 indicates that our elderly patients, all with at least one major associated illness, did not tolerate radical peritoneal debridement. All five patients over 60 years of age in the RPD group died, whereas only two of six such patients in the STD group died. Furthermore, if the over 60-year-old patients are deleted, there remains no statistical difference in survival among the under 60-year-old RPD and STD patients.

An analysis of impact of treatment according to duration of disease further suggests that RPD adversely influenced patients with protracted causes of peritonitis. Eight of 22 RPD patients had historical data consistent with pre-existent peritonitis for greater than 72 hours before the operation. Five of these patients died. Eleven of 24 STD patients had pre-existent peritonitis for more than 72 hours but only three of these patients died.

Further evidence of comparability among the patients randomized to each treatment group is identified in those 14 patients randomized but without bacterial peritonitis. Of nine RPD randomized nonperitonitis patients, two died, while one patient of five nonperitonitis STD patients died.

TABLE 3. Causes of Peritonitis

Treatment Plan	RPD	STD
Number of patients	22	24
Perforated peptic ulcer	9	11
Complicated perforative appendicitis	4	5
Small-large bowel perforation	8	7
Other	1	1

TABLE 4. Bacterial Isolates

Treatment Plan	RPD	STD
Aerobic bacteria	20	26
<i>E. coli</i>	8	9
<i>Klebsiella-Enterobacter</i>	6	10
Group D <i>Streptococcus</i>	2	4
Other	4	3
Anaerobic bacteria	26	17
<i>Bacteroides</i> sp.	12	9
<i>Clostridium</i> sp.	7	5
Others	7	3
Total	46	43

### Discussion

A specific series of events occurs following chemical or bacteriologic contamination of the peritoneal cavity. Among these events, increased vascular permeability of the inflamed tissue results in extravasation of edema fluid and plasma proteins into the area. Teleologically, the vascular permeability change allows ready access of cellular and humoral host defense components to the area of contamination. The combination of leukocytes, fibrin, and bacteria from the fibrinopurulent exudate is characteristic of patients with bacterial peritonitis. The fibrinous exudate may serve as a barrier between areas of suppuration and adjacent areas and becomes a critical component of an abdominal abscess wall. At other times, this exudate occurs over bowel and peritoneal surfaces not in association with specific abscess. The necessity, wisdom or value of removing the fibrinopurulent "peel" is the fundamental question raised by the radical peritoneal debridement concept.

The conventional treatment of intra-abdominal infection has specific goals; namely, repair of the mechanical defect responsible for the contamination, drainage of purulent collections, and debridement of nonviable tissue. One of the purposes of mechanical treatment is certainly to reduce the bacterial burden that is responsible for the active infection. However, it is not realistic to think that mechanical means alone will eliminate the pathogens in intra-abdominal sepsis. Perhaps a more realistic concept of drainage and debridement in the surgical management of infection is that they destroy the environment that promotes bacterial proliferation and invasive infection. Pus and

TABLE 5. Outcome

Treatment Plan	RPD	STD
Died	7	7
peritonitis	5	6
pneumonia	1	1
other	1	0
Reoperation for intraperitoneal infection	5	4

nonviable tissue are relatively inaccessible for cellular and humoral host defense mechanisms. The ability of antibiotics to penetrate these infected areas of compromised blood supply is surely limited. Once these adverse environments have been mechanically eliminated, the residual bacterial contamination must be dealt with by host defense and antibiotic therapy. Those patients whose nonspecific host defenses cannot deal with this residual infection may not benefit from lengthy attempts to remove the remaining bacterial contaminant with a surgical knife.

The data from this report of a prospective, randomized trial of radical peritoneal debridement shows no benefit in survival nor reduction in the frequency of reoperation for abscess between the patients in the two treatment groups. The patients were similar with respect to fundamental pathology, age, associated illnesses, and bacterial pathogens. Antibiotic therapy and peritoneal irrigation were constant between the two groups. These data further suggest that elderly patients tolerated radical peritoneal debridement poorly as indicated by uniform death of patients in the RPD group over 60 years of age.

The problem of management of the residual bacterial contaminant within the peritoneal cavity remains a formidable one. Systemic antibiotic therapy has been disappointing in affecting the natural history of severe peritonitis.<sup>4,17</sup>

This has led to additional efforts to find more powerful drugs to serve this purpose. Concern about anaerobic bacteria has resulted in the addition of powerful and dangerous antibiotics to treat *Bacteroides fragilis* in peritoneal infections. Prospective data is not available to support that premise, and previous retrospective data has demonstrated no value of such antibiotic therapy.<sup>8,20</sup> Direct application of antibiotics<sup>18</sup> and antiseptics<sup>5</sup> into the peritoneal cavity has had its advocates but again unequivocal data to support the value of local instillation of antimicrobial chemotherapy is lacking.

Our experience differs from that reported by Hudspeth and it could well be that this population difference contributes to the apparent discrepancy. In his original report, Hudspeth indicated that 92% of his patients had associated intestinal obstruction,<sup>11</sup> a complication absent in the vast majority of our patients. The timing issue, noted above, may also be a factor, there being, as Hau and associates have postulated,<sup>9</sup> a time when, in theory, removal of fibrinous exudates may be either harmful or helpful. While for the moment our experience weighs against the mood application of RPD, it may be that more precise timing and classification of the illness will disclose a group of patients truly benefited by the meticulous application of this concept.

While it is fashionable to seek global explanations

for failure of control of infection, many obvious clinical trials in this common illness remain to be carefully done. These trials may well be dependent on a valid classification of illness with respect to both degree of microbial contamination and temporal evaluation of the peritoneal response. Furthermore, much remains to be clarified about the apparently protective, possibly harmful aspects of certain components of the basic host response to peritoneal contamination.

### Acknowledgments

The authors wish to express their personal indebtedness to the resident surgeons and faculty colleagues in the Department of Surgery at the University of Louisville for their careful and meticulous contributions to this trial and to Laura Trachtenberg, M.S. for her organizational efforts.

### References

1. Ahrenholz DH, Simmons RL. Fibrin in peritonitis: I. Beneficial and adverse effects of fibrin in experimental *E. coli* peritonitis. *Surgery* 1980; 88:41.
2. Altmeier WA. Bodily response to infectious agents. *JAMA* 1967; 202:1085.
3. Altmeier WA, Hummel RP, Hill EO, Lewis S. Changing patterns in surgical infections. *Ann Surg* 1973; 178:436.
4. Artz CP, Barnett WO, Grogan JB. Further studies concerning the pathogenesis and treatment of peritonitis. *Ann Surg* 1962; 155:756.
5. Browne MK, Stoller JL. Intraperitoneal noxythiolin in faecal peritonitis. *Br J Surg* 1970; 57:525.
6. Dalton, AC, Courtney RA, Miller HH. Peritonitis treated with prolonged, intermittent peritoneal lavage. *JAMA* 1969; 207:1345.
7. DiVincenti FC, Cohn I, Jr. Prolonged administration of intraperitoneal Kanamycin in the treatment of peritonitis. *Am Surg* 1971; 37:177.
8. Fry DE, Garrison RN, Polk HC Jr. Clinical implications in bacteroides bacteremia. *Surg Gynecol Obstet* 1979; 149:189.
9. Hau T, Ahrenholz DH, Simmons RL. Secondary bacterial peritonitis: The biologic basis of treatment. *Curr Probl Surg* 1979; 16:1-65.
10. Hau T, Hoffman R, Simmons RL. Mechanisms of the adjuvant effect of hemoglobin in experimental peritonitis. I. In vivo inhibition of peritoneal leukocytosis. *Surgery* 1978; 83:223.
11. Hudspeth AS. Radical surgical debridement in the treatment of advanced generalized bacterial peritonitis. *Arch Surg* 1975; 110:1233.
12. Lee JT, Jr. Mechanisms of the adjuvant effect of hemoglobin in experimental peritonitis. V. The significance of the coordinated iron component. *Surgery* 1979; 86:41.
13. McKenna JP, Currie DJ, MacDonald JA, et al. The use of continuous postoperative peritoneal lavage in the management of diffuse peritonitis. *Surg Gynecol Obstet* 1970; 130:254.
14. McMullan MH, Barnett WO. The clinical use of intraperitoneal cephalothin. *Surgery* 1970; 67:432.
15. Noon GP, Beall AC Jr, Jordan GL Jr, et al. Clinical evaluation of peritoneal irrigation with antibiotic solution. *Surgery* 1967; 62:73.
16. Polk HC, Jr. Generalized peritonitis: A continuing challenge. *Surgery* 1979; 86:777.
17. Stephen M, Loewenthal J. Generalized infective peritonitis. *Surg Gynecol Obstet* 1978; 147:231.
18. Stephen M, Loewenthal J. Continuing peritoneal lavage in high-risk peritonitis. *Surgery* 1979; 85:603.
19. Stone HH, Guest BS, Geheber CE, Kolb LD. Cefamandole in treatment of peritonitis. *J Infect Dis* 1978; 137:S103.
20. Stone HH, Kolb LD, Geheber CE. Incidence and significance of intraperitoneal anaerobic bacteria. *Ann Surg* 1975; 181:705.